Citation:

Djoussé L, Gaziano JM. Egg consumption in relation to cardiovascular disease and mortality: the Physicians' Health Study. *Am J Clin Nutr.* 2008 Apr;87(4):964-9.

PubMed ID: 18400720

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the association between egg consumption and the risk of CVD and mortality.

Inclusion Criteria:

- Male
- Aged 40-85 years
- American
- Physicians
- Physicians' Health Study (PHS) I participant
- Completed forms concerning egg consumption

*A detailed description of the PHS I has been published previously, refer to *N Engl J Med* 1989;321:129–35 (PubMed: 2664509)

Exclusion Criteria:

History of:

- stroke
- gout
- myocardial infarction
- transient ischemic attack
- cancer (except nonmelanoma skin cancer)
- peptic ulcer
- current liver or kidney disease
- current use of trial treatments

Description of Study Protocol:

Recruitment The current project used data from the Physicians' Health Study (PHS) I.

Design - Prospective cohort study of 21,327 American male physicians

Blinding used: PHS1 was double-blind, placebo-controlled trial.

Intervention: Not applicable, but also low-dose aspirin and beta-carotene treatment. Hazards Ratio adjusted for treatment group.

Statistical Analysis:

- Time-dependent Cox regression model
- Cox proportional hazard models (using 10% change in hazard ratio)
- Regression model
- Stratified analyses
- Significance level was set at 0.05

Data Collection Summary:

Timing of Measurements

Information on egg consumption obtained at baseline, 24, 48, 72, 96 and 120 months.

Dependent Variables

- Risk of CVD
- Risk for total mortality

Independent Variables

- Egg intake - semiquantitative food frequency questionnaire
- Participants were asked to report how often, on average, they have eaten eggs (one) during the past year". Possible response categories included "rarely/never", "1-3/month", "1/week", "2-4/week", "5-6/week", "daily", and "2+/day".

Control Variables

- Age
- BMI
- Smoking
- History of hypertension
- Hypercholesterolemia
- Parental history of premature myocardial infarction
- Diabetes mellitus
- Atrial fibrillation
- Breakfast cereals
- Alcohol consumption
- Vegetable consumption
- Use of multivitamin
- Physical activity

Description of Actual Data Sample:

Initial N: 33,223 males, 0 females. At the end of the run-in period, 22,071 subjects were randomized to low-dose aspirin, beta-carotene, both agents, or placebo.

Attrition (final N): 21,327 males, 0 females. Exclusion of 834 subjects was due to missing data on egg consumption (n=151) or covariates (n=683).

Age: 40-85 years, mean age = 53.7 ± 9.5 years

Other relevant demographics: physicians

Anthropometrics

Characteristics of 21,327 participants according to categories of egg consumption in the Physicians' Health Study:

Body mass index (kg/m^2):

<1 egg/week = 24.5±2.6

1 egg/week = 24.7±2.7

2-4 egg/week = 24.9±2.7

5-6 1 egg/week = 25.2±2.9

+71 egg/week = 25.0±3.2 <0.0001

Location: United States of America

Summary of Results:

Key Findings:

- After an average follow-up of 20 years, a total of 1,550 new myocardial infarction, 1,342 incident strokes, and 5,169 deaths occurred in the cohort
- Frequent consumption of eggs was associated with older age; higher body mass index; higher consumption of vegetables and lower frequency of breakfast cereal consumption; higher proportion of current drinkers and smokers, and users of multivitamins; higher prevalence of diabetes and hypertension; and lower prevalence of exercise, hypercholesterolemia, and parental history of premature CHD.
- While egg consumption of up to 6 eggs per week was not associated with the risk of all-cause mortality, consumption of 7 or more eggs per week was associated with a 23% increased risk of death after controlling for confounders (P for trend < 0.0001).
- In a stratified analysis, history of diabetes at baseline, there was a stronger and statistically significant association between egg consumption and all-cause mortality among subjects with prevalent diabetes than those without diabetes.
- Compared with the lowest category of egg consumption, intake of 7+ per week was associated with 22% increased risk of death in the absence of prevalent diabetes whereas a 2-fold increased risk of death was observed in the presence of prevalent diabetes (p for interaction between diabetes and egg consumption was 0.029 in the parsimonious model and 0.09 in the multivariable adjusted model.

Other findings:

- In multivariable Cox regression model, egg consumption was not associated with incident myocardial infarction, total stroke or types of stroke.
- History of hypercholesterolemia at baseline did not influence the relation between egg consumption and MI, stroke, or total deaths.

From the lowest to the highest category of egg consumption, multivariable adjusted hazard ratios (95% CI) for ischemic stroke were respectively:

- 1.0
- 1.03 (0.86-1.23)
- 1.08 (0.91-1.28)
- 1.11 (0.86-1.43)
- 0.99 (0.78-1.26)
- *(p for trend 0.74).

From the lowest to the highest category of egg consumption, multivariable adjusted hazard ratios (95% CI) for hemorrhagic stroke were respectively:

- 1.0
- 0.66 (0.44-1.00)
- 0.92 (0.63-1.36)
- 1.29 (0.76-2.20)
- 1.07 (0.65-1.78)

*(p for trend 0.11).

From the lowest to the highest category of egg consumption, multivariable adjusted hazard ratios (95% CI) for MI without diabetes were respectively:

- 1.0; 1.07 (0.92-1.25)
- 1.16 (0.99-1.34)
- 1.13 (0.90-1.42)
- 0.91 (0.73-1.14)

From the lowest to the highest category of egg consumption, multivariable adjusted hazard ratios (95% CI) for MI with diabetes were respectively:

- 1.0; 1.39 (0.61-3.21)
- 1.45 (0.64-3.28)
- 1.82 (0.66-5.03)
- 1.06 (0.43-2.64)

*(p for trend 0.93 and p for interaction 0.48).

From the lowest to the highest category of egg consumption, multivariable adjusted hazard ratios (95% CI) for stroke were, for subjects without diabetes were respectively:

- 1.0; 0.94 (0.80-1.11)
- 1.07 (0.91-1.25); 1.12 (0.88-1.42)
- 0.96 (0.77-1.21)

*(p for trend 0.42)

From the lowest to the highest category of egg consumption, multivariable adjusted hazard ratios (95% CI) for stroke were, for subjects with diabetes were respectively:

- 1.0; 1.95 (0.89-4.30)
- 1.61 (0.72-3.56)
- 1.69 (0.58-4.91)
- 1.83 (0.71-4.23)

*(p for trend 0.52)

Author Conclusion:

Our data suggest that infrequent egg consumption does not influence the risk of CVD and only confers a modest increased risk for total mortality in male physicians. In addition, egg consumption was positively related to mortality and such relation was stronger among diabetic subjects in this selective population.

Reviewer Comments:

Study substituted missing values at baseline using reported egg consumption at 24 months in 113 individuals. Authors note the following limitations:

- *We cannot exclude unmeasured confounding or residual confounding as possible explanation of the observed positive association among diabetic subjects*
- *We were not able to examine the effects of saturated fat, markers of insulin resistance, lipids and other nutrients or relevant biomarkers on the observed association*
- *Lack of detailed dietary questionnaire data prevented us from controlling for energy and other major nutrients*
- *Sample consists of male physicians who may have different behaviors than the general population limits generalizability of the findings*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes

4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes

7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes